Claims 2 and 78, 79, and 81 depend from claim 1, claims 4-5, 35, and 37 depend from claim 3, and claims 86-93 depend from claim 85 and are patentable over EP '215 for the reasons stated with respect to claims 1, 3, and 85 and by reason of the additional requirements which they introduce.

II. 35 U.S.C. 103(a)

A. EP 0248215 in combination with Hawley's Condensed Chemical Dictionary

Reconsideration is requested of the rejection of claims 1-5, 35, 37, and 78-93 under 35 U.S.C. 103 as being unpatentable over EP '215 taken with Hawley's Condensed Chemical Dictionary ("Hawley's").

As stated in greater detail above in Section I, claims 1, 3, and 85, as amended, are directed to methods of treating an organism for a condition mediated by COX-2 expression.

EP '215 merely teaches the use of the extract disclosed therein to treat hyperprolactinemia, and as discussed above, does not anticipate the presently claimed invention as the reference does not demonstrate the administration of the extract disclosed therein to an organism suffering from a condition mediated by the expression of COX-2, the administration of the compound in a COX-2 inhibiting amount, or the use of the compound to inhibit COX-2.

Hawley's merely demonstrates that methylene chloride (dichloromethane) can be used for solvent extraction. It does not demonstrate the use of the solvent to extract *Vitex agnus castus*.

Therefore, even when combined, the two references still fail to teach or suggest all the claim limitations of the rejected claims, as the references do not teach the administration of the extract disclosed therein to an organism having a condition mediated by the expression of COX-2, the administration of the compound in a COX-2 inhibiting amount, or the use of the compound to inhibit COX-2. Because the combination of references fails to teach or suggest all such claim limitations, the Office has failed to establish a *prima facie* case of obviousness.[1]

Claims 2 and 78-84 depend from claim 1, claims 4-5, 35, and 37 depend from claim 3, and claims 86-93 depend from claim 85 and are patentable over EP '215 in combination with Hawley's for the reasons stated with respect to claims 1, 3, and 85 and by reason of the additional requirements which they introduce.

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[1] MPEP §2142.

B. JP 200236835 in combination with EP 0248215 and Hawley's Condensed Chemical Dictionary

Reconsideration is requested of the rejection of claims 1-5, 35, 37, and 78-93 under 35 U.S.C. 103, as being unpatentable over JP 200236835 ("JP '835") in view of EP '215 and Hawley's.

As stated in greater detail above in Section I, claims 1, 3, and 85, as amended, are directed to methods of treating an organism for a condition mediated by COX-2 expression.

The full abstract of JP '835, enclosed herewith, discloses a composition comprising Koto-sugi as the "main raw material" and five other secondary components, one of which is *Vitex agnus castus* rhizomes. JP '835 does not disclose whether the *Vitex agnus castus* compound is the active compound, and more importantly whether this compound is present in sufficient amounts to inhibit COX-2 mediated conditions as required by the present claims. Furthermore, because there are many different components and pathways affecting cancer, it is unclear from the abstract of JP '835 whether the composition disclosed therein is used to treat the COX-2 mediated component of cancer.

For the reasons stated above in Section II.A., the combination of EP '215 and Hawley's does not render the present invention obvious. The defects of this combination are not cured by the addition of JP '835. When combined, the three references still fail to teach or suggest all the claim limitations of the rejected claims, as the references do not disclose administration of the extract in an amount sufficient to inhibit COX-2 to an organism suffering from a condition mediated by COX-2 expression or the inhibition of the COX-2 mediated component of cancer. Because the combination of references fails to teach or suggest all such claim limitations, the Office has failed to establish a *prima facie* case of obviousness.[2]

Furthermore, the mere fact that a composition is asserted to have the ability to prevent cancer is not necessarily indicative of the fact that the composition selectively inhibits COX-2 activity. The Office cites Subbaramaih, et al.[3] for the proposition that resveratrol can be used to inhibit cyclooxygenase-2 transcription in human mammary epithelial cells, asserting that it "is well known in the art that inhibiting COX-2 is an important strategy in treating cancer." While

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[2] MPEP §2142.

[3] Subbaramaih, et al, "Resveratrol inhibits cyclooxygenase-2 transcription in human mammary epithelial cells", Ann. N.Y. Acad. Sci., 1999, Vol. 889, pp. 214-223, disclosed as Reference No. 76 in Applicants' IDS filed January 8, 2002.

this may be true, this reference fails to cure the aforementioned defects present in the JP '835, as well as in the combination of references.

There is a myriad of compositions, both of synthetic and of natural origin, which have chemotherapeutic effects. These compositions achieve such results through a number of different pathways. Because of the variety in compounds and pathways, there is simply no basis within JP '835 to presumptively attribute the alleged chemotherapeutic benefits of the composition disclosed therein to COX-2 inhibition.

Furthermore, the Office offers no evidence in support of its position. There is no reason to believe that the ability of resveratrol, a chemopreventive agent found in grapes, to inhibit COX-2 is indicative of the ability of the composition disclosed in JP '835 to inhibit the same. Instead, the Office has combined these references to allege obviousness based upon an "obvious to try" standard, a standard that has been rejected under 35 U.S.C. 103.[4] Therefore, the Office has failed to establish a *prima facie* case of obviousness.

Claims 2 and 78-84 depend from claim 1, claims 4-5, 35, and 37 depend from claim 3, and claims 86-93 depend from claim 85 and are patentable over JP '835 in combination with EP '215 and Hawley's for the reasons stated with respect to claims 1, 3, and 85 and by reason of the additional requirements which they introduce.

Applicants and their undersigned counsel acknowledge and thank Examiner Meller for the courtesy extended during the October 25, 2002, interview. During this interview, the references, as well as the amendments and arguments presented herein, were discussed. No agreement was reached with respect to the patentability of any claim.

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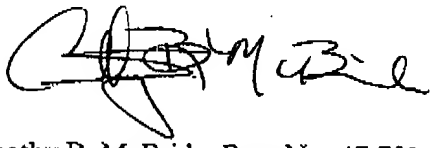
[4] *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q. 2d 1529, 1532 (Fed. Cir. 1988); *In re Yates*, 663 F.2d 1054, 1057, 211 U.S.P.Q. 1149, 1151 (C.C.P.A. 1981).

CONCLUSION

In light of the above arguments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-5, 35, 37, 78, 79, 81, and 85-93 under 35 U.S.C. 102(b) and of claims 1-5, 35, 37, and 78-93 under 35 U.S.C. 103(a).

Applicant requests an extension of time to and including December 15, 2002, for filing a response to the above-mentioned Office action. The Commissioner is hereby authorized to charge the applicable extension fee to Deposit Account No. 19-1345.

Respectfully submitted,



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Version With Markings To Show Changes Made

The Claims have been amended as follows:

1. (amended) A method [for selective inhibition of COX-2 in] of treating an organism for a condition which is mediated by COX-2 expression, the method comprising the step of administering to the organism a composition comprising a therapeutically or prophylactically effective COX-2 inhibiting amount of an organic extract of an edible plant, wherein the extract selectively inhibits the activity of COX-2 relative to COX-1, and the inhibitory effect of the extract on COX-2 activity is greater than or equal to about 2 times greater than the inhibitory effect of the extract on COX-1 activity as determined in vitro by an IC_{50} ratio of COX-1/COX-2.

2. (amended) The method of claim 1 wherein the inhibitory effect of the extract on COX-2 activity is greater than or equal to about 10 times greater than the inhibitory effect of the extract on COX-1 activity.

3. (amended) A method [for inhibiting the activity of COX-2 in] of treating an organism for a condition which is mediated by COX-2 expression, the method comprising the step of administering to the organism a composition comprising a therapeutically or prophylactically effective COX-2 inhibiting amount of an organic extract of an edible plant, wherein the plant is selected from the orders consisting of Agavales, Apocynales, Arales, Aristolochiales, Asterales, Brassicales, Cactales, Caryophyllales, Cucurbitales, Elaeagnales, Fagales, Gnetales, Graminales, Lamiales, Liliales, Malvales, Musales, Myrtales, Papaverales, Plantaginales, Polemoniales, Ranales, Rosales, Rubiales, Rutales, Scrophulariales, Umbellales, Urticales, and Violales.

85. (amended) A method of treating or preventing COX-2 mediated inflammation or an inflammation-associated disorder in an organism with a condition which is mediated by COX-2 expression, the method comprising administering to the organism a composition comprising a therapeutically or prophylactically effective COX-2 inhibiting amount of the purified composition according to claim 78.